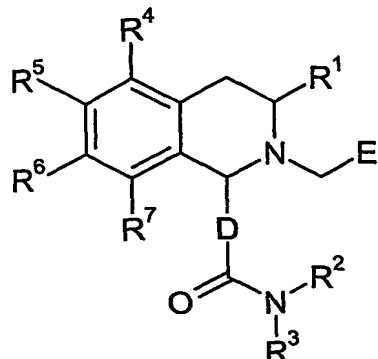


What is claimed is:

1. A compound of formula I, a pharmaceutically acceptable salt thereof, diastereomers, enantiomers, or mixtures thereof:



5

wherein

$R^1$  is selected from  $-H$  and  $C_{1-6}$ alkyl;

$R^2$  and  $R^3$  are independently selected from  $-H$  and  $C_{1-6}$ alkyl;

$R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,  $C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocycl-l-oxy,  $C_{3-6}$ heterocycl-l-C<sub>1-4</sub>alkoxy,  $C_{6-10}$ aryl-oxy,  $C_{6-10}$ aryl-C<sub>1-4</sub>alkoxy,  $C_{1-6}$ alkyl-S(=O)<sub>2</sub>-O-,  $C_{6-10}$ aryl-S(=O)<sub>2</sub>-O-,  $C_{1-6}$ alkyl-NH-S(=O)<sub>2</sub>-O-, and  $(C_{1-6}$ alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent groups selected from  $R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said  $C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocycl-l-oxy,  $C_{3-6}$ heterocycl-l-C<sub>1-4</sub>alkoxy,  $C_{6-10}$ aryl-oxy,  $C_{6-10}$ aryl-C<sub>1-4</sub>alkoxy,  $C_{1-6}$ alkyl-S(=O)<sub>2</sub>-O-,  $C_{6-10}$ aryl-S(=O)<sub>2</sub>-O-,  $C_{1-6}$ alkyl-NH-S(=O)<sub>2</sub>-O-, and  $(C_{1-6}$ alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen,  $C_{1-3}$ alkoxy,  $-OH$ ,  $-NO_2$ ,  $C_{1-3}$ alkyl,  $-NH_2$ , and  $-CO_2-C_{1-3}$ alkyl;

E is a 5-membered heterocycl optional substituted with one or more groups selected from halogen,  $C_{1-6}$ alkyl,  $-C(=O)-O-C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{6-10}$ aryl-C<sub>1-4</sub>alkyl, and  $C_{6-10}$ aryl-S(=O)<sub>2</sub>-; and

D is a divalent group comprising a benzene ring.

25

2. A compound according to claim 1, wherein

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$R^1$  is selected from  $-H$  and  $C_{1-3}\text{alkyl}$ ;

$R^2$  and  $R^3$  are independently  $C_{1-3}\text{alkyl}$ ;

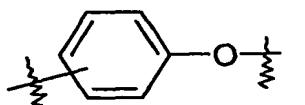
$R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,

$C_{1-6}\text{alkyl}$ , phenyl,  $C_{1-6}\text{alkoxy}$ ,  $C_{3-6}\text{cycloalkoxy}$ , tetrahydropyranyloxy, pyridinyloxy,

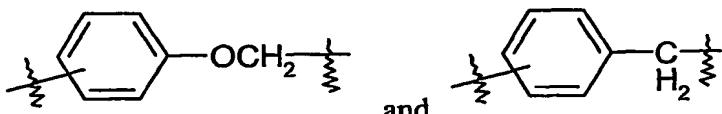
5 morpholinyloxy, tetrahydropyranyl- $C_{1-4}\text{alkoxy}$ , pyridinyl- $C_{1-4}\text{alkoxy}$ , morpholinyl- $C_{1-4}\text{alkoxy}$ , phenoxy, benzyloxy,  $C_{1-6}\text{alkyl-S(=O)_2-O-}$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}\text{alkyl-NH-S(=O)_2-O-}$ , and  $(C_{1-3}\text{alkyl})_2N-S(=O)_2-O-$ ; or any two adjacent groups selected from  $R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  form a divalent group selected from  $-O-CH_2-O-$  and  $-O-CH_2-CH_2-O-$ , wherein said  $C_{1-6}\text{alkyl}$ , phenyl,  $C_{1-6}\text{alkoxy}$ ,  $C_{3-6}\text{cycloalkoxy}$ ,

10 tetrahydropyranyloxy, pyridinyloxy, morpholinyloxy, tetrahydropyranyl- $C_{1-4}\text{alkoxy}$ , pyridinyl- $C_{1-4}\text{alkoxy}$ , morpholinyl- $C_{1-4}\text{alkoxy}$ , phenoxy, benzyloxy,  $C_{1-6}\text{alkyl-S(=O)_2-O-}$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}\text{alkyl-NH-S(=O)_2-O-}$ , and  $(C_{1-3}\text{alkyl})_2N-S(=O)_2-O-$  are optionally substituted with one or more groups selected from halogen, methoxy,  $-OH$ ,  $-NO_2$ , and  $C_{1-3}\text{alkyl}$ ;

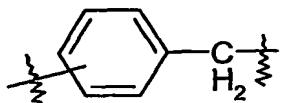
15  $E$  is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more groups selected from halogen,  $C_{1-4}\text{alkyl}$ ,  $-C(=O)-O-C_{1-3}\text{alkyl}$ , phenyl, benzyl, and benzenesulfonyl; and



D is selected from phenylene, pyridylene,



, and



20

3. A compound according to claim 1,

wherein

$R^1$  is selected from  $-H$  and methyl;

$R^2$  and  $R^3$  are selected from ethyl and isopropyl;

$R^4$ ,  $R^5$  and  $R^6$  are independently selected from  $-H$ ,  $-OH$ , halogen,  $-NO_2$ ,

$C_{1-6}\text{alkyl}$ , phenyl,  $C_{1-6}\text{alkoxy}$ ,  $C_{3-6}\text{cycloalkoxy}$ , tetrahydropyranyloxy, pyridinyloxy,

morpholinyloxy, tetrahydropyranyl- $C_{1-4}\text{alkoxy}$ , pyridinyl- $C_{1-4}\text{alkoxy}$ , morpholinyl-

$C_{1-4}\text{alkoxy}$ , phenoxy, benzyloxy,  $C_{1-6}\text{alkyl-S(=O)_2-O-}$ , phenyl- $S(=O)_2-O-$ ,  $C_{1-3}\text{alkyl}$

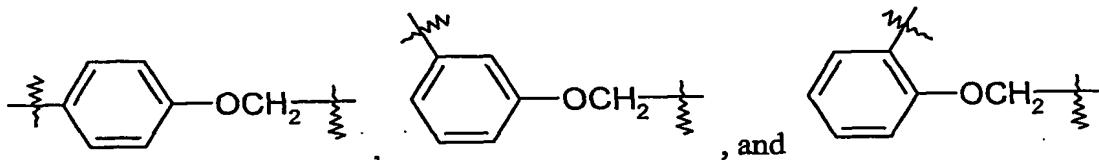
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NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-3</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> form -O-CH<sub>2</sub>-O-, wherein said phenoxy, benzyloxy, and phenyl-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen and methoxy;

5 R<sup>7</sup> is selected from -H and C<sub>1-3</sub>alkoxy;

E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more groups selected from halogen, C<sub>1-4</sub>alkyl, -C(=O)-O-C<sub>1-3</sub>alkyl, phenyl, benzyl, and benzenesulfonyl; and

10 D is selected from *para*-phenylene, *para*-benzylene,



4. A compound according to claim 1, wherein

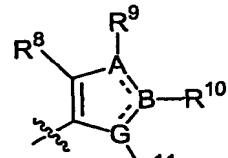
R<sup>1</sup> is selected from -H and methyl;

15 R<sup>2</sup> and R<sup>3</sup> are ethyl;

R<sup>4</sup> is selected from -H, NO<sub>2</sub> and methoxy, R<sup>5</sup> is selected from -H, -Br, -F, -OH, methoxy, methylsulfonyloxy, N,N-dimethylsulfamylloxy, and R<sup>6</sup> is selected from -H, -OH, -NO<sub>2</sub>, methoxy, ethoxy, isopropylloxy, neopentylloxy, cyclobutylloxy, 4-tetrahydro-2H-pyranylloxy, 2-(4-morpholino)ethoxy, benzyloxy, phenoxy, 4-

20 fluorophenoxy, 3-methoxyphenoxy, 4-methoxyphenoxy, 3-pyridinylloxy, methanesulfonyloxy, benzenesulfonyloxy, dimethylsulfamylloxy; or any two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> form -O-CH<sub>2</sub>-O-;

R<sup>7</sup> is selected from -H and methoxy;



E is , wherein A and B are independently selected from C, N

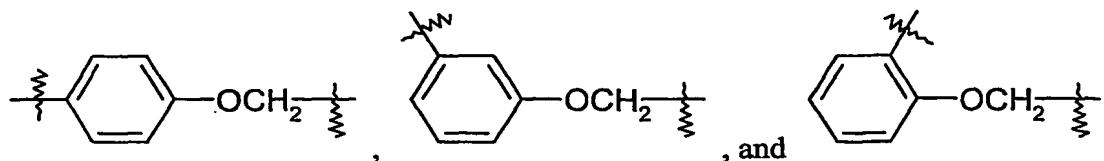
25 and S, and G is selected from C, N, O and S with a proviso that at least one of A, B and G is C, at most one of A, B and G is S and one of the bonds between A and B, and between B and G is a double bond;

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wherein R<sup>8</sup> is selected from -H, -Cl, methyl, -CO<sub>2</sub>Me and phenyl; R<sup>9</sup> is selected from -H and methyl; R<sup>10</sup> is selected from -H, methyl, n-butyl and phenyl; R<sup>11</sup> is selected from -H, methyl, benzyl and benzenesulfonyl.

D is selected from *para*-phenylene, *para*-benzylene,

5



5. A compound selected from:

COMPOUND 12.1.1: N,N-Diethyl-2-{{[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}benzamide

10 COMPOUND 12.1.2: 2-{{[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.3: N,N-Diethyl-3-{{[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}benzamide

15 COMPOUND 12.1.4: 3-{{[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.5: N,N-Diethyl-4-{{[2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}benzamide

COMPOUND 12.1.6: 4-{{[6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}-N,N-diethylbenzamide

20 COMPOUND 12.1.7: 2-{{[6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.8: 4-{{[6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]methyl}-N,N-diethylbenzamide

25 COMPOUND 12.1.9: 4-{{[6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}N,N-diethylbenzamide

COMPOUND 12.1.10: N,N-Diethyl-4-{{[6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.11: N,N-Diethyl-4-{{[7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

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COMPOUND 12.1.12: N,N-Diethyl-4-{2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.13: 4-{2-[(2-Butyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

5 COMPOUND 12.1.14: 4-{2-[(2-Butyl-4-chloro-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.15: 4-{6,7-Dimethoxy-2-[(2-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

10 COMPOUND 12.1.16: 4-{6,7-Dimethoxy-2-[(3-phenyl-1H-pyrazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.17: 4-(6,7-Dimethoxy-2-{{1-(phenylsulfonyl)-1H-pyrrol-2-yl)methyl}-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.18: N,N-Diethyl-4-{2-[(2-ethyl-4-methyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

15 COMPOUND 12.1.19: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.20: 4-{5,8-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

20 COMPOUND 12.1.21: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]benzamide

COMPOUND 12.1.22: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.23: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

25 COMPOUND 12.1.24: 4-{6,7-Dimethoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.25: N,N-Diethyl-4-{6-methoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.26: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

30 COMPOUND 12.1.27: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.28: 4-{2-[(1-Benzyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.29: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

5 COMPOUND 12.1.30: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.31: 4-{(6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}-N,N-diethylbenzamide

10 COMPOUND 12.1.32: 4-{(6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl}-N,N-diethylbenzamide

COMPOUND 12.1.33: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

COMPOUND 12.1.34: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

15 COMPOUND 12.1.35: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.36: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.37: 4-{2-[(2,5-Dimethyl-1,3-thiazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.38: 4-{6,7-Dimethoxy-2-[(2-phenyl-1,3-thiazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.39: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

25 COMPOUND 12.1.40: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(2-morpholin-4-ylethoxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.41: 4-{7-Ethoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.42: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.43: N,N-Diethyl-4-{6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.44: N,N-Diethyl-4-{7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.45: Methyl 5-{{1-[(4-[(diethylamino)carbonyl]phenyl)-6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl]methyl}-1H-imidazole-4-carboxylate

5 COMPOUND 12.1.46: 1-{{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl methanesulfonate

COMPOUND 12.1.47: N,N-Diethyl-4-{6-[(4-methyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

10 COMPOUND 12.1.48: N,N-Diethyl-4-{6-[(2-phenyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

COMPOUND 12.1.49: 4-{6-Bromo-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

15 COMPOUND 12.1.50: 4-{6-Bromo-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.51: 4-{6,7-Dimethoxy-3-methyl-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.52: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

20 COMPOUND 12.1.53: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-7-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.54: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-5-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

25 COMPOUND 12.1.55: N,N-Diethyl-4-{7-[(4-methyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.56: N,N-Diethyl-4-{7-[(2-phenyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.57: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

30 COMPOUND 12.1.58: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.59: 4-{7-(Cyclobutyloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.60: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(neopentyloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

5 COMPOUND 12.1.61: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.62: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

10 COMPOUND 12.1.63: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl dimethylsulfamate

COMPOUND 13.1.1: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(tetrahydro-2H-pyran-4-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

15 COMPOUND 14.1.1: N,N-Diethyl-4-{6-methoxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.2: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

20 COMPOUND 14.1.3: N,N-diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.4: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.5: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

25 COMPOUND 14.1.6: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(pyridin-3-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 15.1.1: 4-{7-(Benzylloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

30 COMPOUND 16.4.1: N,N-Diethyl-4-{6-methoxy-7-(3-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.2: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.3: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl benzenesulfonate

COMPOUND 17.1.1: 4-{6,7-Dihydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

5 COMPOUND 17.1.2: N,N-Diethyl-4-{6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.3: N,N-Diethyl-4-{7-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

10 COMPOUND 17.1.4: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 17.1.5: N,N-Diethyl-4-{7-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.6: N,N-Diethyl-4-{6-hydroxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

15 COMPOUND 17.1.7: N,N-Diethyl-4-{6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.8: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

20 COMPOUND 17.1.9: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 18.1.1: 4-{2-[(1,4-Dimethyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 18.1.2: 4-{2-[(1,5-Dimethyl-1H-imidazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

25 COMPOUND 19.1.1: 4-{7-Ethoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.1.1: 4-{(1S)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

30 COMPOUND 20.2.1: 4-{(1R)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.1.2: N,N-Diethyl-4-{(1S)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 20.2.2: N,N-Diethyl-4-{(1R)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

5 COMPOUND 20.1.3: N,N-Diethyl-4-{(1S)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 20.2.3: N,N-Diethyl-4-{(1R)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

10 COMPOUND 20.1.4: N,N-Diethyl-4-{(1S)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 20.2.4: N,N-Diethyl-4-{(1R)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 20.1.5: N,N-Diethyl-4-{(1S)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

15 COMPOUND 20.2.5: N,N-Diethyl-4-{(1R)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 20.1.6: N,N-Diethyl-4-{(1S)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

20 COMPOUND 20.2.6: N,N-Diethyl-4-{(1R)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 20.1.7: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 20.2.7: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

25 COMPOUND 20.1.8: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide

COMPOUND 20.2.8: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]-benzamide;  
and pharmaceutically acceptable salts thereof.

30

6. A compound according to any one of claims 1-5 for use as a medicament.

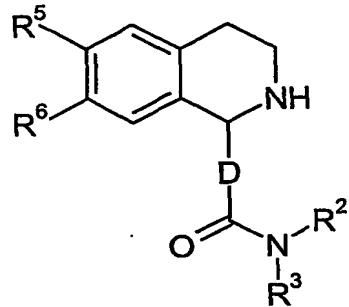
7. The use of a compound according to any one of claims 1-5 in the manufacture of a medicament for the therapy of pain, anxiety or functional gastrointestinal disorders.

5 8. A pharmaceutical composition comprising a compound according to any one of claims 1-5 and a pharmaceutically acceptable carrier.

9. A method for the therapy of pain in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective 10 amount of a compound according to any one of claims 1-5.

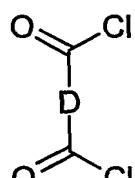
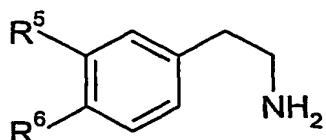
10. A method for the therapy of functional gastrointestinal disorders in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to any one of 15 claims 1-5.

11. A process for preparing a compound of formula II,



II

20 comprising of the step of reacting a compound of formula III with a compound of formula IV in the presence of  $\text{HNR}^2\text{R}^3$ :

IIIIV

,

wherein

$R^2$  and  $R^3$  are independently selected from -H and  $C_{1-6}$ alkyl;

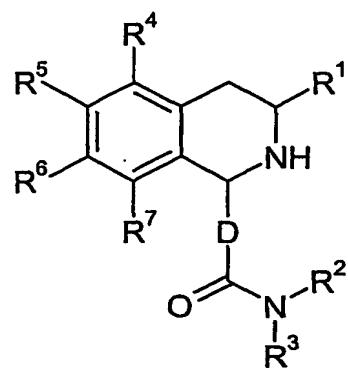
$R^5$  and  $R^6$  are independently selected from -H, -OH, halogen, - $NO_2$ ,  $C_{1-6}$ alkyl,

5  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocycl- $oxy$ ,  $C_{3-6}$ heterocycl- $yl$ -  
 $C_{1-4}$ alkoxy,  $C_{6-10}$ aryl- $oxy$ ,  $C_{6-10}$ aryl- $C_{1-4}$ alkoxy,  $C_{1-6}$ alkyl- $S(=O)_2-O-$ ,  $C_{6-10}$ aryl-  
 $S(=O)_2-O-$ ,  $C_{1-6}$ alkyl- $NH-S(=O)_2-O-$ , and  $(C_{1-6}$ alkyl) $_2N-S(=O)_2-O-$ ; or  $R^5$  and  $R^6$   
together form a portion of a 5 or 6-membered ring that fused with the benzene ring of  
formula I, wherein said  $C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocycl- $oxy$ ,  $C_{1-6}$ heterocycl- $yl$ - $C_{1-4}$ alkoxy,  $C_{6-10}$ aryl- $oxy$ ,  $C_{6-10}$ aryl- $C_{1-4}$ alkoxy,  $C_{1-6}$ alkyl- $S(=O)_2-O-$ ,  $C_{6-10}$ aryl- $S(=O)_2-O-$ ,  $C_{1-6}$ alkyl- $NH-S(=O)_2-O-$ , and  
 $(C_{1-6}$ alkyl) $_2N-S(=O)_2-O-$  are optionally substituted with one or more groups selected  
from halogen,  $C_{1-3}$ alkoxy, -OH, - $NO_2$ ,  $C_{1-3}$ alkyl, - $NH_2$ , and - $CO_2-C_{1-3}$ alkyl; and  
D is a divalent group comprising a benzene ring.

10

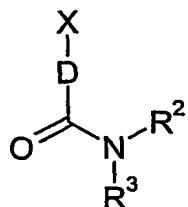
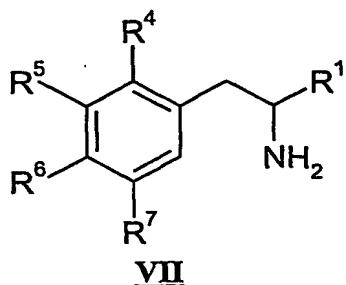
15

12. A process for preparing a compound of formula V,

V

comprising of the step of reacting a compound of formula VI with a

20 compound of formula VII in the presence of an acid catalyst:

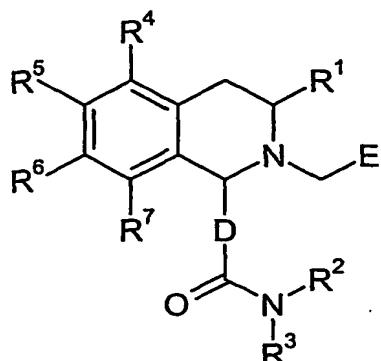
**VI****VII**

, wherein

X is selected from  $-\text{CH}(\text{OEt})_2$ ,  $=\text{CHOMe}$  and  $-\text{CHO}$ ;5 R<sup>1</sup> is selected from  $-\text{H}$  and C<sub>1-6</sub>alkyl;R<sup>2</sup> and R<sup>3</sup> are independently selected from  $-\text{H}$  and C<sub>1-6</sub>alkyl;10 R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently selected from  $-\text{H}$ ,  $-\text{OH}$ , halogen,  $-\text{NO}_2$ ,C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocycl-l-oxy, ..15 C<sub>3-6</sub>heterocycl-l-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-,C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any20 two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C<sub>1-6</sub>alkyl,C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocycl-l-oxy, C<sub>3-6</sub>heterocycl-l-25 C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally25 substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy,  $-\text{OH}$ ,  $-\text{NO}_2$ ,C<sub>1-3</sub>alkyl,  $-\text{NH}_2$ , and  $-\text{CO}_2-\text{C}_1-\text{3alkyl}$ ; and

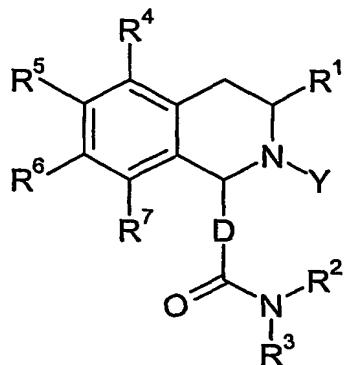
D is a divalent group comprising a benzene ring.

20 13. A process for preparing a compound of formula I,



I

comprising: reacting a compound of formula VIII with E-CHO:



VIII

5

wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R<sup>1</sup> is selected from -H and C<sub>1-6</sub>alkyl;

R<sup>2</sup> and R<sup>3</sup> are independently selected from -H and C<sub>1-6</sub>alkyl;

R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently selected from -H, -OH, halogen, -NO<sub>2</sub>,

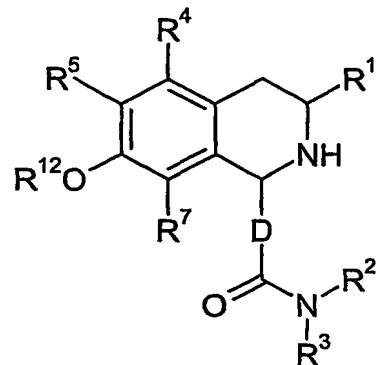
10 C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocycl-l-oxy, C<sub>3-6</sub>heterocycl-l-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent groups selected from R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C<sub>1-6</sub>alkyl,

15 C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocycl-l-oxy, C<sub>3-6</sub>heterocycl-l-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy, -OH, -NO<sub>2</sub>, C<sub>1-3</sub>alkyl, -NH<sub>2</sub>, and -CO<sub>2</sub>-C<sub>1-3</sub>alkyl;

20 E is a 5-membered heterocycl optionally substituted with one or more groups selected from halogen, C<sub>1-6</sub>alkyl, -C(=O)-O-C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkyl, and C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-; and

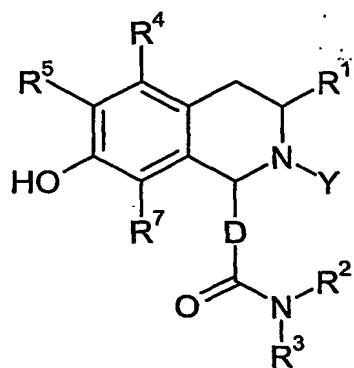
D is a divalent group comprising a benzene ring.

## 14. A process for preparing a compound of formula IX,

**IX**

comprising: reacting a compound of formula X with R¹²-OH or R¹²-B(OH)₂:

5

**X**

, wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R¹² is selected from C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkyl,

10 C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkyl, C<sub>6-10</sub>aryl, and C<sub>3-6</sub>heteroaryl, wherein said C<sub>6-10</sub>aryl, C<sub>3-6</sub>heterocyclyl and C<sub>3-6</sub>heteroaryl are optionally substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy, -OH, -NO<sub>2</sub>, C<sub>1-3</sub>alkyl, -NH<sub>2</sub> and -CO<sub>2</sub>-C<sub>1-3</sub>alkyl; and

R¹ is selected from -H and C<sub>1-6</sub>alkyl;15 R² and R³ are independently selected from -H and C<sub>1-6</sub>alkyl;

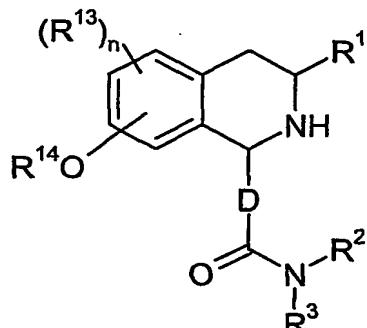
R⁴, R⁵, and R⁷ are independently selected from -H, -OH, halogen, -NO<sub>2</sub>, C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocyclyl-oxy, C<sub>3-6</sub>heterocyclyl-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-,

$C_{6-10}$ aryl-S(=O)<sub>2</sub>-O-,  $C_{1-6}$ alkyl-NH-S(=O)<sub>2</sub>-O-, and  $(C_{1-6}$ alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or  $R^4$  and  $R^5$  together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said  $C_{1-6}$ alkyl,  $C_{6-10}$ aryl,  $C_{1-6}$ alkoxy,  $C_{3-6}$ cycloalkoxy,  $C_{3-6}$ heterocycl-*oxy*,  $C_{3-6}$ heterocycl- $C_{1-4}$ alkoxy,  $C_{6-10}$ aryl-*oxy*,  $C_{6-10}$ aryl- $C_{1-4}$ alkoxy,

5  $C_{1-6}$ alkyl-S(=O)<sub>2</sub>-O-,  $C_{6-10}$ aryl-S(=O)<sub>2</sub>-O-,  $C_{1-6}$ alkyl-NH-S(=O)<sub>2</sub>-O-, and  $(C_{1-6}$ alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen,  $C_{1-3}$ alkoxy, -OH, -NO<sub>2</sub>,  $C_{1-3}$ alkyl, -NH<sub>2</sub>, and -CO<sub>2</sub>- $C_{1-3}$ alkyl; and

D is a divalent group comprising a benzene ring.

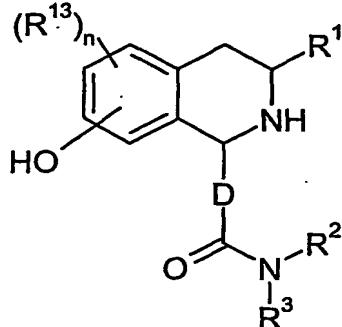
10 15. A process for preparing a compound of formula XI,



XI

comprising:

reacting a compound of formula XII with NsCl, NsBr, or (CF<sub>3</sub>CO)<sub>2</sub>O to  
 15 protect the =NH group of formula XI;  
 reacting the protected compound with R<sup>14</sup>-Y<sup>1</sup> followed by deprotecting the =NH group:



XII

wherein

n is 0, 1, 2 or 3;

each R<sup>13</sup> is independently selected from -H, -OH, halogen, -NO<sub>2</sub>, C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocycl-l-oxy, C<sub>3-6</sub>heterocycl-l-  
5 C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy, C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O-; or any two adjacent R<sup>13</sup> form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, C<sub>3-6</sub>heterocycl-l-oxy, C<sub>3-6</sub>heterocycl-l-C<sub>1-4</sub>alkoxy, C<sub>6-10</sub>aryl-oxy, C<sub>6-10</sub>aryl-C<sub>1-4</sub>alkoxy,  
10 C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-O-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-O-, C<sub>1-6</sub>alkyl-NH-S(=O)<sub>2</sub>-O-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-O- are optionally substituted with one or more groups selected from halogen, C<sub>1-3</sub>alkoxy, -OH, -NO<sub>2</sub>, C<sub>1-3</sub>alkyl, -NH<sub>2</sub>, and -CO<sub>2</sub>-C<sub>1-3</sub>alkyl;;

Y<sup>1</sup> is halogen;

R<sup>14</sup> is selected from C<sub>1-6</sub>alkyl-S(=O)<sub>2</sub>-, C<sub>6-10</sub>aryl-S(=O)<sub>2</sub>-, C<sub>1-6</sub>alkyl-NH-  
15 S(=O)<sub>2</sub>-, and (C<sub>1-6</sub>alkyl)<sub>2</sub>N-S(=O)<sub>2</sub>-,

R<sup>1</sup> is selected from -H and C<sub>1-6</sub>alkyl;

R<sup>2</sup> and R<sup>3</sup> are independently selected from -H and C<sub>1-6</sub>alkyl; and

D is a divalent group comprising a benzene ring.